

***Remarks***

Applicant respectfully requests that the above amendments be entered after final as they place the claims in better form for allowance.

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 2 and 6-8 are pending in the application, with 2 being the independent claim. Claim 2 has been amended. Support for the amendment can be found in the specification at page 14, lines 6-11. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Obviousness-type Double Patenting***

The Examiner has rejected claims 2 and 6-8 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,183,974. (Paper No. 8, page 2, item 4). The Examiner states that, "Applicant has failed to identify that limitation in the instant claims which is not met by the patent claim."  
*Id.*

Applicants respectfully travers this rejection, however, request that it be held in abeyance until the remaining outstanding issues in this application are resolved and the claims are otherwise in condition for allowance.

***Rejections under 35 U.S.C. § 112***

The Examiner maintained the rejection of claims 2 and 6-8 under 35. U.S.C. § 112, second paragraph for allegedly being incomplete for omitting essential elements, such omission amounting to a gap between the elements." Applicants' respectfully traverse this rejection.

The Examiner maintains that the Applicants have failed "to explain how one can distinguish between a compound which effects either of the two measured pathways directly or through a mechanism other than a heterologous receptor..." (Paper No. 9, page 3). The Examiner suggests that "some comparative step between a cell comprising the recombinant receptor and a cell lacking that receptor would be a minimal requirement for the claimed method to meets [*sic*] its functional requirements." *Id.* Applicants' maintain that one of skill in the art who was practicing the invention would perform the appropriate experimental controls and therefore there is no gap in the claim language. Contrary to the Examiner's assertion, the claim is complete.

Solely in an effort to expedite prosecution, however, and without acquiescence in the propriety of the rejection, Applicants have amended claim 2, from which claims 6-8 depend, to include in step (d) "contacting said stably transfected cells and cells of step (a), which do

not express said receptor of step (b), with said compound of interest." Thus, the rejection is moot and Applicants respectfully request that it be withdrawn.

***Rejections under 35 U.S.C. § 101***

The Examiner has maintained his rejection of claims 2 and 6 to 8, under 35 U.S.C. § 101 alleging that the invention is "inoperative and therefore lacks utility." (Paper No. 8, page 3). Applicants respectfully traverse this rejection.

The Examiner argues that due to the 35 U.S.C. § 112, second paragraph rejection, the invention is inoperative. However, in light of the previously described amendment of claim 2, this rejection is now moot and should be withdrawn.

***Rejections under 35 U.S.C. § 103(a)***

The Examiner has maintained the rejection of claims 2 and 6-8 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Catanzariti *et al. BioTechniques* 15:474-479 (1993) ("Catanzariti"), and in view of the combination of the U.S. Patent 5,494,806 to Segre *et al.* ("Segre") and the Bringhurst *et al. Endocrinology* 132:2090-2098 (1993) publication ("Bringhurst"). Applicants' respectfully traverse this ground of rejection.

The Examiner further noted that the rejection was maintained for the reasons of record in "section 6 of Paper Number 4." Applicants were unable to find Paper No. 4 and assume that the Examiner actually meant section 6 of Paper 13. If Applicants are incorrect in this assumption they request that the Examiner further elaborate on this matter.

It is noted that the Examiner does not dispute that the Applicants' have discovered unexpected properties that could ***not*** have been predicted from the prior art. (Paper No. 8, pages 3-4). However, the Examiner alleges that "the properties identified by Applicant[s] were ***entirely inherent*** to that assay system which was described in the Bringhurst *et al.* publication...." (Paper No. 8, page 4) (Emphasis added). Applicants respectfully disagree.

The sole rebuttal to Applicants' arguments in the reply filed April 18, 2002 appears to be that Applicants' invention is inherent to the assay of Bringhurst. Therefore, it appears that the rejection is now based s only on that single piece of cited art, i.e. Bringhurst. Applicants have reached this conclusion because nothing more is being said about the remaining cited art in rebuttal to Applicants previous arguments.

In any event, a rejection based on alleged inherence of Applicants' invention is incorrect for several reasons. First, in *Jones v. Hardy* (220USPQ 1021 (Fed. Cir. 1984) the court concluded that "anticipation by inherence" was being confused with obviousness which are separate and distinct. It is submitted that the same error has taken place in the current rejection. Thus, the Examiner has provided no legal basis for an obviousness rejection based on inherence. Applicants respectfully request such support.

Second, even if the rejection could be correctly based on inherency, the disclosure in Bringhurst does not rise to the level where inherency can be established. In order for a reference to inherently "anticipate" an invention, the result must "necessarily" flow from the cited art. This has not been shown.

The Examiner has done no more than make a conclusory statement that "properties identified by Applicant were inherent to that assay system," i.e. Bringhurst's. More is necessary. Applicants respectfully request the Examiner to specifically cite those sections

of Bringhurst that establish the alleged inherency. If no such support can be pointed out or if the Examiner cannot show such inherency based on something already known in the art, the rejection cannot stand.

Concerning the remaining art cited at the beginning of the rejection but for which there is no elaboration, Applicants assume that they are not part of the current rejection. If, however, they are still part of the rejection, Applicants reiterate from the reply dated April 18, 2002, that Catanzariti is entirely focused on the use of the u-PA response in LLC-PK1 cells to detect responses mediated by receptors coupled to *only* Gs not to *both* Gs and Gq. There is nothing in Catanzariti that teaches or suggests Applicants' method for screening compounds which involves agonists or antagonists of receptors that couple to *both* Gs and Gq proteins. If Applicants have overlooked such a reference, the Examiner is respectfully requested to point it out.

Segre also fails to teach that the human PHT receptor is a dual-signaling receptor. If there is no such teaching, how could one of skill in the art arrive at Applicants' claimed invention.

The Examiner stated that "in the instant case the claimed method and the prior art method both comprise those same unexpected properties identified by the Applicant[s]." (Paper No. 8, page 4). However, the Examiner fails to provide any examples of how the prior art conveys the notion that the receptors could be coupled to two distinct pathways. Applicants respectfully request that the Examiner provide such examples.

The Examiner's entire argument is based on inference. Therefore, "The Examiner must provide rationale or evidence tending to show inherency." *See* M.P.E.P. 2112. "To establish inference, the extrinsic evidence 'must make clear that the missing descriptive

matter is *necessarily* present in the thing described in the reference and that it would be so recognized by persons of ordinary skill.'" (citations omitted). No such evidence has been provided. The mere possibility that something *may* be inherent is not sufficient to establish inherence.

Further, there is no evidence that the instant invention would have been obvious to one of skill in the art in view of Bringhurst without the knowledge contained in the Applicants' application. Therefore, such the rejection is based on inappropriate hindsight.

The Examiner cites *In re Dillon* to attempt to make the point that the "discovery that claimed composition possesses property not disclosed for prior art does not alone defeat prima facie case." *See In re Dillon*, 16 USPQ2d 1897 (Fed. Cir. 1990). *Dillon* is not dispositive to the Applicants' invention

However, even if one attempts to to rely upon the teachings of *Dillon*, one would come to the conclusion that "[t]here is no objective teaching in the prior art that would have led one of ordinary skill to make this product in order to solve the problem that was confronting [the Applicant]." *Id.* 718. The Examiner has pointed to no basis in the prior art to suggest that a single receptor, coupled to both Gs and Gq existed. Therefore, the combination of the cited art could not have suggested the use of a method to screen agonist and antagonists of an unknown receptor.

Finally, the Examiner cites several cases (*In re Dillon*, *In re Linter*, and *Ex parte Levengood*) to make the point that the prior art need only provide motivation to make the claimed invention, but not necessarily for the same reason or to achieve the same result as the Applicant. However, Applicants refer the Examiner to *In re Vaeck*, in which claims were rendered non-obvious over the prior art because "the prior art in this case offers no

suggestion, explicit or implicit, of the substitution that is the difference between the claimed invention and the prior art." *In re Vaeck*, 947 F.2d 495 (1991). Applicants argue that the current invention is also non-obvious in light of the prior art as it offers no suggestion of a method to screen for agonists or antagonists of a single receptor that couples to both Gs and Gq proteins.

Further, the Examiner refers to *Levengood* for the proposition that "while there must be a motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention." Absence is not clear why the Examiner has stated this since the rejection appears to be based on alleged inherence. In any event, the Examiner has provided no motivation whatsoever in the office action, to make the claimed invention. Applicants specifically request the Examiner to state any "motivation" for making the claimed invention that is found in the cited art. In the absence of such a motivation the rejection cannot stand and must be withdrawn.

In light of the above arguments the rejection has been overcome and should be withdrawn.

### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite

prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,



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**Version with markings to show changes made**

2. (thrice amended) A method for determining whether a compound of interest affects an adenylyl cyclase or phospholipase C pathway and therefore is an agonist or antagonist of a receptor which couples to both Gs and Gq proteins comprising:

- (a) providing a cell line which expresses urokinase-type plasminogen activator (u-PA);
- (b) providing an expression vector comprising a nucleotide sequence encoding for a receptor which couples to both Gs and Gq proteins, said receptor not normally expressed in said cell line of step (a);
- (c) introducing said expression vector into said cell line, thereby providing stably transfected cells;
- (d) contacting said stably transfected cells and cells of step (a), which do not express said receptor of step (b), with said compound of interest; and
- (e) measuring the u-PA activity of the cell culture supernatant of said cells of step (d) by fluorescence or absorbency spectroscopy, thereby determining whether said compound of interest is an agonist or antagonist of a receptor which couples to Gq and Gs proteins.